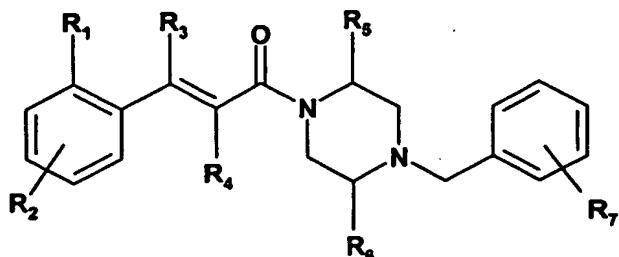


CLAIMS

1. A compound of formula i, or a pharmaceutically acceptable salt or ester thereof,



wherein

R₁ is -X-R₁₀, -X-(R₁₀)₂ or -NR₁₁R₁₂

Wherein X is a linker comprising 1 atom or a chain comprising 2, 3 or 4 atoms selected from N, C, O or S, and wherein when said linker comprises 2 or more C atoms the linker may comprise 1 or more C=C or C≡C bonds;

wherein any of said atoms has up to 2 optional substituents selected from hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, sulfur amino;

R₁₀ is a substituent independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, cycloalkyl, heterocycloalkyl, aryl, heteroaryl;

R₁₁ and R₁₂ each represent a lower alkyl group connected together such that R₁ is an optionally substituted heterocycloalkyl or heteroaryl group;

R₂ and R₇ represent one or more substituents attached to the phenyl ring selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl;

- 156 -

R₃ and R₄ are independently selected from the group consisting of hydrogen, cyano, halo, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl;

R₅ and R₆ are independently selected from the group consisting of hydrogen, cyano, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on X are one or more independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, amino, sulfur, sulfinyl, sulfonyl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, oxy, lower alkyl, lower alkyenyl, lower alkynyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R₁₀ are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, Sulfur, cycloalkyl, heterocycloalkyl, aryl; Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, Sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, Sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R₁₁ and R₁₂ are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R₂ and R₃ are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R₃ and R₄ are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo,

nitro, oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R₅ and R₆ are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, hydroxyl, optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl, imino, oxime;

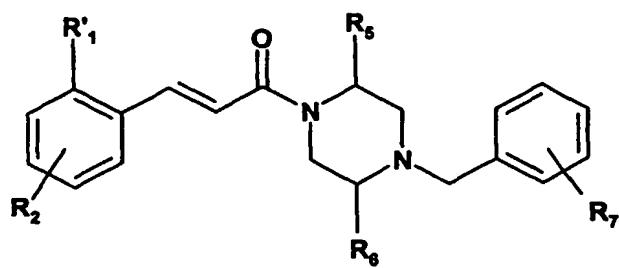
Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, hydroxyl, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

2. a compound of formula II, or a pharmaceutically acceptable salt or ester thereof,



Wherein

R'₁ is -X'-R'₁₀

Wherein X' is a linker independently selected from optionally substituted -N-C-N-, -N-C-, -N-S-, -N-S-N-, -C-N-, -S-N-, -C≡C-, -C=C-, -N-C-S-, -C-, -S-N-S-R'₁₀.

Wherein R₂ – R₁₀ are as herein before defined.

R'₁₀ is one or more substituents independently selected from the group consisting of hydrogen, halo, or optionally substituted carbonyl, amino, heterocycloalkyl and aryl.

when R'₁ is -N-C-N-R'₁₀ the C atom is substituted by oxo, =N-C≡N or =C-NO₂.

when R'₁ is -N-C-N-R'₁₀, R'₁₀ is Hydrogen.

when R'₁ is -N-C-N-R'₁₀, R'₁₀ is optionally substituted by hydrogen.

when R'₁ is -N-C-R'₁₀ or -C-N-R'₁₀ the C atom is substituted by oxo.

when R'₁ is -N-C-R'₁₀ or -C-N-R'₁₀, R'₁₀ is optionally substituted methyl, piperidinyl, imidazolidinyl, pyrrolidinyl, morpholino.

when R'₁ is -N-C-R'₁₀ or -C-N-R'₁₀, R'₁₀ is substituted by hydrogen, methyl, benzyl, acetyl, oxo, dimethylamino, isopropyl, hydroxy, formic acid ethyl ester.

when R'₁ is -N-S-R'₁₀ or R'₁₀-S-N-S-R'₁₀ the S atom or atoms are substituted twice by oxo.

when R'₁ is -N-S-R'₁₀ or R'₁₀-S-N-S-R'₁₀, R'₁₀ is optionally substituted methyl.

when R'₁ is -N-S-R'₁₀ or R'₁₀-S-N-S-R'₁₀, R'₁₀ is optionally substituted by hydrogen.

when R'₁ is -N-S-N-R'₁₀ the S atom is substituted twice by oxo and the N atom is independently optionally substituted by methyl.

when R'₁ is -N-S-N-R'₁₀, R'₁₀ is hydrogen or optionally substituted methyl, imidazolyl, thiazolyl.

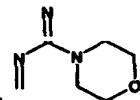
when R'₁ is -N-S-N-R'₁₀, R'₁₀ is optionally substituted by hydrogen, methyl, acetamidyl.

when R'₁ is -C≡C-R'₁₀, R'₁₀ is optionally substituted methyl, isopropyl or piperindinyl

when R'₁ is -C≡C-R'₁₀, R'₁₀ is optionally substituted by hydrogen or amine

when R'₁ is -C=C-R'₁₀, R'₁₀ is optionally substituted piperidinyl

when R'₁ is -C=C-R'₁₀, R'₁₀ is optionally substituted by hydroxy, methyl.



when R'₁ is -N-C-S-R'₁₀ the C atom is substituted by =N-C≡N or

when R'₁ is -N-C-S-R'₁₀, R'₁₀ is optionally substituted methyl

when R'₁ is -N-C-S-R'₁₀, R'₁₀ is optionally substituted by hydrogen.

when R'₁ is -C-R'₁₀ the C atom is optionally substituted by oxo,

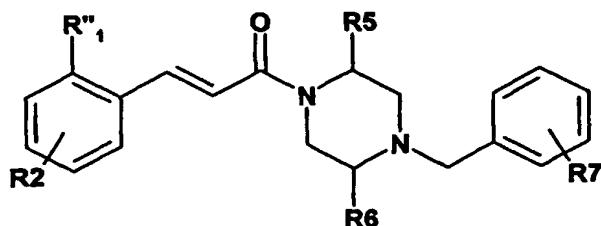
when R'₁ is -C-R'₁₀, R'₁₀ is 3-oxa-1-aza-spiro[4.4]nonan-2-one, hydroxy, optionally substituted pyrrolidinyl, morpholino, piperazinyl, formic acid methyl ester, [1,2,4]triazol, imidazolidinyl, tetrazolyl, -N(CH₃)OCH₃ or methoxy.

when R'₁ is -C-R'₁₀, R'₁₀ is optionally substituted by hydrogen, oxo, methyl, acetyl, isopropyl, methoxy, hydroxy, formic acid methyl ester, dimethylamino or ethanone.

The optional substituents on R'₁₀ are one or more substituents independently selected from the group consisting of hydrogen, or optionally substituted oxy, lower alkyl, carbonyl, amino; Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, or optionally substituted oxy;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen or optionally substituted lower alkyl;

3. A compound of formula IIa, or a pharmaceutically acceptable salt or ester thereof,



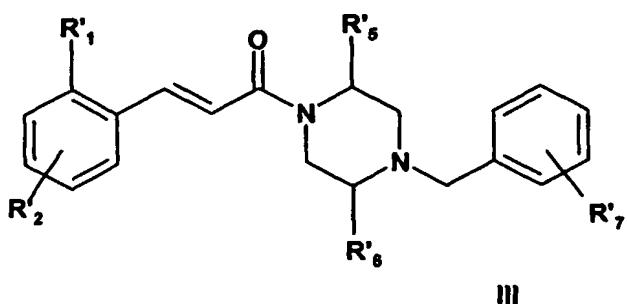
IIa

Wherein

R''_1 is $-NR''_{11}R''_{12}$

Wherein $-NR''_{11}R''_{12}$ collectively represents imidazolidinyl-2,4-dione, optionally substituted once or twice by a lower alkyl group.

4. A compound of formula III, or a pharmaceutically acceptable salt or ester thereof,



Wherein R'_1 is as herein before defined.

R'_2 and R'_7 are hydrogen, cyano, halo, butadienyl, methoxy, ethoxy, 2-methoxyethoxy, morpholino, trifluoromethoxy, 2-methylpropoxy, 2-propoxy.

R'_5 and R'_6 are independently selected from the group consisting of hydrogen and lower alkyl, acetyl;

5. A compound according to claim 1 selected from the examples 1-113 as disclosed in the specification.

6. A method of inhibiting chemokine receptors or of reducing inflammation in a subject (i.e., a mammal, especially a human) in need of such treatment which method comprises administering to said subject an effective amount of a compound according to claim 1, or a method of treating any of the above mentioned conditions, particularly a method of treating an inflammatory or autoimmune disease or condition, e.g., multiple sclerosis or rheumatoid arthritis, or alleviating one or more symptoms of any of the above mentioned conditions;

- 162 -

a compound according to claim 1 for use as a pharmaceutical, e.g. for use as an immunosuppressant or antiinflammatory agent or for use in the prevention, amelioration or treatment of any disease or condition as described above, e.g., an autoimmune or inflammatory disease or condition;

A pharmaceutical composition comprising a compound according to claim 1 in association with a pharmaceutically acceptable diluent or carrier, e.g., for use as an immunosuppressant or anti-inflammatory agent or for use in the prevention, amelioration or treatment of any disease or condition as described above, e.g., an autoimmune or inflammatory disease or condition, or

use of a compound according to claim 1 in the manufacture of a medicament for use as an immunosuppressant or anti-inflammatory agent or for use in the prevention, amelioration or treatment of any disease or condition as described above, e.g., an autoimmune or inflammatory disease or condition.

7. A process for the preparation of a compound of formula I.

8. All novel compounds, methods, processes and uses substantially as hereinbefore described with particular reference to the Examples.